DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Manuel J. Quinones, M.D.
800 Pacific Coast Highway, #181
Redondo Beach, CA 90277

Ref: 09-HFD-45-02-05

Dear Dr. Quinones:

Between July 21 and August 5, 2008, Ms. Diane C. Van Leeuwen and Mr. Richard W. Tubb, representing the Food and Drug Administration (FDA), conducted an investigation and met with you to review your conduct of a clinical investigation [Protocol Number (b) (4) entitled "A Randomized, Double-Study to compare the Durability of Glucose Lowering and Preservation of Pancreatic Beta-cell Function of Rosiglitazone Monotherapy Compared to Metformin or Glyburide/Glibenclamide in Patients with Drug-Naïve, recently Diagnosed Type 2 Diabetes Mellitus"] of the investigational drug rosiglitazone (Avandia), performed for SmithKline Beecham/GlaxoSmithKline (GSK).

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to evaluate the conduct of research and to ensure that the rights, safety, and welfare of the human subjects of the study have been protected.

From our review of the establishment inspection report and the documents submitted with that report, we conclude that you did not adhere to the applicable statutory requirements and FDA regulations governing the conduct of clinical investigations and the protection of human subjects. We are aware that at the conclusion of the inspection, Ms. Van Leeuwen and Mr. Tubb presented and discussed with you Form FDA 483, Inspectional Observations. We wish to emphasize the following:

1. **You failed to assure that an IRB that complies with the requirements set forth in 21 CFR part 56 was responsible for the initial and continuing review and approval of the proposed clinical study (21 CFR 312.66).**

   Specifically, IRB approval lapsed on several occasions during the ongoing study where subjects were being treated or seen for follow-up visits. Inspection found that the study was initiated on 4/27/00 and was closed in approximately 2006. Some trial subjects

participated and were monitored for up to four years. We note that you failed to have IRB approval from 4/27/01 to 5/28/01, 4/8/04 to 9/8/04, and 9/9/05 to 11/27/05.

2. **You failed to maintain adequate and accurate case histories that record all observations and data pertinent to the investigation [21 CFR 312.62(b)].**

   a. Subject #79878 was initially consented with an English version of the informed consent form, and later reconsented with a Spanish version, under a different subject number (#81439). The two source charts for this subject had conflicting dates of birth (b) (6) vs. (b) (6)), dates of type II diabetes mellitus diagnosis (10/99 vs. 8/00), and smoking history (30 yrs 1 cigar a day vs. none).

   b. Protocol-required chest x-rays were missing for the following subjects:
      i. #80292 reported taken on 12/22/00
      ii. #80295 reported taken on 2/15/01
      iii. #80294 reported taken on 2/2/01
      iv. #80293 reported taken on 1/25/01

   c. Chest x-ray report for subject #81700 was missing for x-rays dated 7/13/01.

3. **You failed to ensure the investigation was conducted according to the investigational plan (21 CFR 312.60).**

   The protocol required a Drug Receipt Form to be used to record all delivered medication lot numbers, quantity shipped and date of receipt. The first drug shipment was received 6/28/00; the last shipment was received 1/31/06. However, the required records were not kept for the period prior to 11/21/03.

This letter is not intended to be an all-inclusive list of deficiencies with your clinical study of an investigational drug. It is your responsibility to ensure adherence to each requirement of the law and relevant FDA regulations. You should address these deficiencies and establish procedures to ensure that any on-going or future studies will be in compliance with FDA regulations.

Within fifteen (15) working days of your receipt of this letter, you should notify this office in writing of the actions you have taken or will be taking to prevent similar violations in the future. Failure to adequately and promptly explain the violations noted above may result in regulatory action without further notice.

If you have any questions, please contact Constance Lewin, M.D., M.P.H., at 301-796-3397; FAX 301-847-8748. Your written response and any pertinent documentation should be addressed to:

Constance Lewin, M.D., M.P.H.
Branch Chief, Good Clinical Practice Branch I
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research
Food and Drug Administration
Bldg 51, Room 5354
10903 New Hampshire Avenue
Silver Spring, MD 20993

Sincerely yours,

{See appended electronic signature page}

Leslie K. Ball, M.D.
Director
Division of Scientific Investigations
Office of Compliance
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

LESLIE K BALL
03/03/2009